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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,451	05/15/2000	JONATHAN P MURPHY	PM-268066	2087

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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1634	24

DATE MAILED: 10/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,451	MURPHY ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1630, Art Unit 1634.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 July 2002 has been entered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-12 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They

include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided

The amount of guidance provided is extremely limited and then prophetic.

The Presence or Absence of Working Examples

The specification has been found to contain 8 examples:

- Example 1 – Construction of an enhanced fluorescent form of hGH, pages 11-14;
- Example 2 – Construction of gene by substituting W for F31 and F97, pages 14-16;
- Example 3 – Fluorescence detection, page 16;
- Example 4 – Human Calcitonin, pages 16-17;
- Example 5 – Human Growth Hormone Releasing Factor, page 176;
- Example 6 – Human Insulin, pages 17-18;
- Example 7 – Human Erythropoietin (EPO), page 18; and
- Example 8 – Human Interleukin 2 (IL-2), pages 18-19.

Of the 8 examples, only Example 3 is directed to the claimed method. A review of the disclosure, however, fails to find sufficient guidance for the actual measurement of hGHf, or any other exogenously administered polypeptide, by fluorescent measurement. While the specification has been found to provide suggestions and motivating statements that such could possibly be done, the specification fails to teach in sufficient detail just how the various contemplated sample materials (e.g., blood, saliva, urine, semen and tears (claim 5)) are to be prepared, tested, etc. The specification has not been found to provide any guidance for practicing the claimed method with any mammal.

The claimed method clearly encompasses the measurement of polypeptides that comprise the same fluorescent amino acid residues that are naturally found in the sample. While the claimed method recites the limitation that the exogenously administered polypeptide is to fluoresce more or less than naturally occurring or endogenous polypeptide, the specification is essentially silent s to how one is to measure the fluorescence of an exogenously administered polypeptide that is administered at a level, or dosage, that is less than what is naturally present. Given that the fluorescent moiety is one and the same as that found in the endogenous polypeptide, one is detecting the signal from the same label. The specification is silent as to how one is to somehow correlate the signal from a polypeptide that is endogenous and the signal form an identical "tag" when found on an exogenous polypeptide.

It is further noted that the claimed method does not require the separation of the exogenous polypeptide from the sample, nor is it required that all other polypeptides be removed from the sample prior to any measurement being undertaken. While claim 3 does recite that various forms of separation can be performed, the level of separation is not articulated. Further,

the specification is essentially silent as to how any and all possible exogenously administered polypeptides are to be separated from a sample.

The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. <u>However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art.</u> It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. In support of this position attention is directed to the disclosure of US Patent 4,066,405 (Henkin). As seen in column 2, saliva is recognized in the art as containing a series of proteins that fluoresce as a direct result to the tryptophan present therein. Henkin also teaches that the amount of fluorescence varies as a result to abnormalities. The subject specification, however, is essentially silent as to what degree native fluorescence varies in individuals due to variances and abnormalities in their physiological conditions. Further, the specification is silent as to how these variances are to be taken into consideration when measuring the fluorescence of any exogenously administered polypeptide. The failure of the specification to teach in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention unfairly shifts the burden of enablement from applicant to that of the public. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art is limited to the extent that exogenously administered polypeptides are measured in a mixture of other polypeptides wherein said exogenously

administered polypeptides are to be detected by the presence of a common tag, e.g., the presence of tryptophan. The prior art, however, has advanced to the point that variances in physiological conditions, and with it protein production, have been recognized as have their inherent variances in fluorescence.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Predictability or Unpredictability of the Art

The predictability in the art is quite low as one is trying to detect and differentiate one compound present in a mixture of other compounds wherein the label is ubiquitous and is subject to variation due to normal fluctuations in physiological conditions.

The Breadth of Scope of the Claims

The claims encompass the measurement of any and all exogenously administered polypeptides in any mammalian subject where any type of sample, under any condition, is evaluated. It is further noted that the claimed method encompasses any level of detection/discrimination.

5. In view of the unpredictability of the art, the profound breadth of scope, and the limited guidance provided, the specification has not been found to teach in such full, clear, concise, and

exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

6. Claims 1-12 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims fairly encompass the measurement of any and all possibly exogenously administered polypeptides in any and all possible samples from any and all possible mammals. A review of he disclosure fails to find where an adequate written description has been provided whereby even one exogenously administered polypeptide could be measured in any sample from even one mammal, e.g., a human, much less any mammal. The detail provided within the four corners of the application have not been found to rise to the level of an adequate written description that reasonably suggests that applicant was in possession of the invention at the time of filing. As shown ab0ove, the specification has been found to set forth but one expel that is directed to the claimed invention and then the prophetic example does not describe the claimed invention in sufficient detail so to satisfy the requirements of 35 USC 112, first paragraph, as it relates to the written description. At best, the disclosure could be considered to render obvious some embodiments encompassed by the claims. Suggesting or rendering obvious an invention, however, does not fulfill the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

7. It is well settled that "[I]t is not enough for purposes of written description requirement of Section 112 that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to modification that the inventor might have envisioned, but failed to disclose." *Lockwood v. American Airlines Inc.* (Fed. Cir. March 1997) 41 USQP2d 1961 at 1966.

8. For the above reasons, and in the absence of convincing evidence to the contrary, the claims are rejected 35 USC 112, first paragraph.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

11. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
September 10, 2002